Observation of Hand movements by Older Persons with Dementia: Effects on Cognition: a Pilot Study

Eggermont, L.H.P.; Swaab, D.F.; Hol, E.M.; Scherder, E.J.A.

published in
Dementia and Geriatric Cognitive Disorders
2009

DOI (link to publisher)
10.1159/000209311

document version
Publisher's PDF, also known as Version of record

Original Research Article

Dementia and Geriatric Cognitive Disorders

Dement Geriatr Cogn Disord 2009;27:366–374
DOI: 10.1159/000209311

Accepted: November 21, 2008
Published online: March 24, 2009

Observation of Hand Movements by Older Persons with Dementia: Effects on Cognition

A Pilot Study

Laura H.P. Eggermont[a] Dick F. Swaab[b] Elly M. Hol[b] Erik J.A. Scherder[a, c]

[a]Department of Clinical Neuropsychology, VU University, [b]Netherlands Institute for Neuroscience, Amsterdam, and [c]Institute of Human Movement Sciences, University of Groningen, Groningen, The Netherlands

Key Words
Cognition · Dementia · Hand movements · Motor activity · Nursing homes

Abstract
Background/Aim: Hand movement observation activates mirror neurons, located in brain areas that are vulnerable to Alzheimer's disease. We examined the effects of hand movement observation on cognition in older persons with dementia. ***Methods:*** Nursing home residents with dementia (n = 44) watched either videos showing hand movements or videos showing a documentary for 30 min, 5 days a week, for 6 weeks. Neuropsychological tests were performed at baseline, week 6 and week 12. ***Results:*** Linear mixed model analyses revealed a significant interaction effect on an attention test, but not on cognitive domains. Additional analyses showed that a face recognition task improved significantly. ***Conclusion:*** Although these findings do not support an overall beneficial effect of hand movement observation on cognition in dementia, specific cognitive functions improved. Future studies are warranted.

Introduction

Physical activity is positively associated with cognition in older persons [1]. More specifically, randomized controlled trials in healthy older adults have revealed improved cognition, particularly executive functions such as inhibition and working memory [1]. Although some studies that offer a physical activity intervention (e.g. walking) to older persons with dementia show a beneficial effect on cognition, these studies often show methodological flaws such as no randomization or lack of a control group [2]. Moreover, not every older individual is able to engage in a physical activity such as walking. In general, older persons with dementia constitute a very frail group, especially those living in a nursing home [3]. As opposed to walking, a more suitable form of physical activity may be the performance of more specific tasks, for instance hand movements. This type of motor activity, combined with facial movements, was applied to older persons with Mild Cognitive Impairment (MCI), which resulted in higher scores on tasks that appeal to executive function [4]. The rationale behind this study was that hand movements are known to stimulate areas in the

KARGER

Fax +41 61 306 12 34
E-Mail karger@karger.ch
www.karger.com

1420–8008/09/0274–0366$26.00/0

Accessible online at:
www.karger.com/dem

Laura H.P. Eggermont
VU University, Department of Clinical Neuropsychology
Van der Boechorststraat 1
NL–1081 BT Amsterdam (The Netherlands)
Tel. +31 20 598 8878, Fax +31 20 598 8971, E-Mail LHP.Eggermont@psy.vu.nl

frontal lobe, including the anterior cingulate cortex, which are engaged in sensory, motor and cognitive processes [5]. Unfortunately, it is also the case that hand function is often reduced in aged people as a result of, for instance, rheumatoid arthritis or changes in neural control [6]. Even more so than in healthy older people, fine and gross motor control appears to be affected in older persons with Alzheimer's disease (AD) [7].

It is notable that several brain areas are activated when one executes hand movements, and activation also occurs when one simply observes somebody else performing hand movements. Areas that are able to respond to, for example, hand motor activity executed by others, are believed to contain mirror neurons, and therefore are considered part of a 'mirror-neuron system' [8]. More specifically, mirror neurons are thought to be activated both when a movement is self-produced as well as when a movement is observed when performed by someone else [8]. Evidence for the presence of mirror neurons stems from neuro-imaging studies in cognitively healthy adults linking mirror neurons with empathy processes such as pain perception in others [9] and cognitive process such as learning [10]. Additionally, use of mirror neurons as a rehabilitation strategy has been suggested in stroke and neglect patients [11].

During observation of hand movements, somatotopically organized neural circuits are recruited, just like in the actual execution of hand movements [12]. These areas include the (inferior) parietal lobe, Broca's area, supplementary motor area, dorsal premotor cortex and the superior temporal gyrus [8, 11–13]. Indeed, a well-described brain network connecting frontal, temporal and parietal regions, i.e. the superior longitudinal fasciculus [14] as also established by diffusion tensor imaging [15], is both involved in the mirror neuron system [16] and shows deterioration in AD [17, 18]. Brain areas such as the prefrontal cortex and superior temporal gyrus are specifically known for their involvement in executive function and recognition of faces, respectively [1, 19, 20]. Face recognition is a cognitive function that is extremely important in social contacts [20], disruption of which is a striking and very disabling consequence of dementia [21] and which can be already present in an early stage [22]. In sum, the observation of hand movements activates neural circuits that are involved in cognition and are affected in dementia. This notion makes hand movement observation attractive as a possible treatment strategy for cognitive impairment.

Although cross-sectional studies have shown that it is active rather than passive mental activities that reduce risk for dementia [23, 24], intervention studies offering active mental training to older nursing home residents with dementia show limited cognitive benefits [25, 26]. Additionally, most studies include only limited numbers of participants or do not include a control group [25, 27], rendering tentative positive findings debatable. In view of the nature of the participants and applicability of an intervention, we focus on a more passive mental activity. It is important to realize that mirror neurons could be activated during hand movement observation in 2 conditions: (1) looking at hand movements in real life, and (2) looking at hand movements on video [12]. An intervention that consists of watching a video is relatively simple to apply in a nursing home setting and easily replicated [28]. In the present study, it was examined whether watching a video with purposive actions of hands was beneficial for cognition, in particular face recognition, in older nursing home residents with dementia.

Subjects and Methods

Participants

Seven nursing homes in The Netherlands participated in the study. Possible participants were selected after consultation with the nursing and medical staff. Inclusion criteria used were: (1) age of at least 70 years, and (2) a diagnosis of dementia reported in the medical status. Oral and written consent was obtained from the participants and their relevant relatives or guardians. Approval for this study was granted by the medical ethics committee.

The global level of cognitive functioning was assessed by means of the Mini-Mental State Examination (MMSE) [29]. Individuals were excluded from participation if they had: (1) an MMSE score of <10; (2) an MMSE score of >24; (3) presence of visual disturbances as mentioned in the medical status, reported by the medical staff, or present during the MMSE assessment; (4) hearing difficulties; (5) history of alcoholism; (6) personality disorders; (7) cerebral trauma; (8) hydrocephalus; (9) neoplasm; (10) disturbances of consciousness, and (11) focal brain disorders.

All nursing home residents had received a dementia diagnosis or psychogeriatric indication prior to study onset. Unfortunately, neuro-imaging in the nursing home setting is not performed regularly in The Netherlands. Therefore, specific subtypes of dementia in the current population could not adequately be distinguished. Level of education was determined by a 7-point scale: 1 = did not complete elementary school; 2 = 6 grades of elementary school; 3 = 7 or 8 grades of elementary school; 4 = 3 years of lower general secondary education; 5 = 4 years of lower general secondary education; 6 = pre-university education and higher vocational education; 7 = university and technical college. Comorbid conditions were obtained from the medical status and classified into categories (by L.H.P.E.; table 1). Specific types of medication such as antipsychotics were also recorded. Symptoms of depression were measured by means of a Dutch version of the Geriatric Depression Scale [30]. A higher score indicates more symptoms of depression (maximal score = 30). Level of anxiety was

Table 1. Baseline characteristics

	Exp. group (n = 19)	Control group (n = 25)	t	d.f.	p
Age, years	84.8 ± 5.2	86.4 ± 5.2	–1.02	42	0.31
MMSE score	17.5 ± 5.0	16.5 ± 3.2	0.82	42	0.42
Geriatric Depression Scale score	7.8 ± 4.6	7.8 ± 3.8	–0.03	41	0.97
Symptom Checklist Anxiety score	14.3 ± 5.7	13.9 ± 3.0	0.33	41	0.75

	Exp. group (n = 19)	Control group (n = 25)	$\chi^2(1)$	p
Women	18	24	0.04	0.84
ApoE4 carriers[1]	6	3	2.52	0.11
Cardiovascular disease	15	21	0.19	0.67
Tumors	3	2	0.65	0.42
Gastro-intestinal disease	8	12	0.15	0.70
Locomotion disease	10	13	0.01	0.97
Neuro- and radiculopathy	7	5	1.54	0.21
Renal insufficiency	4	4	0.19	0.67
Pneumonic disease	5	9	0.47	0.50
Endocrine disorders	5	8	0.17	0.68
Perceptual problems	8	11	0.02	0.90
Antidepressants use	6	6	0.31	0.58
Sedatives use	6	6	0.09	0.76
Neuroleptics use	2	9	1.32	0.25
Analgesics use	7	6	0.55	0.46

Data are means ± SD or numbers, as appropriate.

[1] Apolipoprotein genotype could only be determined in 24 participants. Exp. = Experimental.

established by the use of a subscale of a Dutch version of the Symptom Checklist Anxiety [31]. A higher score indicates more symptoms of anxiety (maximal score = 50).

In order to determine apolipoprotein E (ApoE) genotype, buccal swabs were taken by the primary researcher (L.H.P.E.) or a carefully instructed research assistant in the nursing homes by making use of Catch-all™ collection swabs (Epicentre, Madison, Wisc., USA). Two swabs were taken from each participant. Before the swabs were taken, participants were asked to rinse their mouth thoroughly, and afterwards the swabs were left to dry for 30 min. DNA was isolated from the swab according to the method described by Ilveskoski et al. [32]. The nucleotide sequence of primers used was derived from Gioia et al. [33]. ApoE genotype was indicated as ApoE4 allele present or not present.

Intervention

The interventions were performed in small groups with a maximum of 4 participants and took place in a small separate room in the nursing home. Both types of intervention were guided by psychology students. The interventions of both conditions were applied for 30 min, 5 days a week, for 6 weeks. When a participant was unable or unwilling to attend, the intervention was caught up with later that day or on the weekend.

Experimental Condition

In the experimental condition, the participants watched videotapes on which the hands of a person performing creative activities were shown. The videotapes were designed specially for the present study and consisted of 10 different tapes showing various kinds of activities, for instance cooking, painting, flower arranging, work with clay and needlework. The first shot contained an image of the person performing the activity and after that, the focus was entirely on the movements made by the hands. The person performing the hand movements gave short verbal explanations about the activities that were carried out.

Control Condition

To control for social aspects inherent in any group activity and for the visual stimulation by videotapes, a control group was included. In the control condition, participants watched 10 videotapes from a documentary of the Dutch provinces [34]. Images of Dutch cities and rural areas were shown on video; the videos included interviews with residents of the particular province.

To determine whether the videotapes in both conditions were considered equally entertaining, a short questionnaire was assessed directly after the intervention. The questionnaire contained 3 questions, which asked about the level of interest, the level of enjoyment and the level of attention to the videotape.

Assessment of Cognitive Function

An investigator blind to the treatment condition administered all tests directly before (pre-treatment, T1) and directly after the 6-week period (post-treatment, T2), and again after 6 weeks without treatment (delayed, T3). To assess memory and executive function (EF), the following neuropsychological tests were administered.

Memory

This was assessed with 3 tests: face recognition, picture recognition and an 8 words test.

(1) Face recognition. This subtest from the Rivermead Behavioral Memory Test (RBMT) [35] measures visual, nonverbal long-term memory. In this test the participant is shown 5 cards with faces. To make sure the participant has no visual problem, he/she is asked whether the person on the picture is male or female. After a short interval, the participant is asked to recognize the faces shown earlier among 5 other faces. The outcome measure is the number of faces correctly recognized minus the number of faces incorrectly recognized (maximal score = 10).

(2) Picture recognition. This is also a subtest from the RBMT [35] and measures verbal long-term memory. The participant is shown 10 cards with drawings of objects. With each card, the participant is requested to name the object on the card. After a short interval, the participant has to choose between 20 cards with objects and has to point out the objects already shown. The outcome measure is the number of objects correctly recognized minus the number of objects that were incorrectly recognized (maximal score = 20).

(3) Eight words test [36]. During this test the examiner reads out 8 words in a row. This process is repeated 5 times, and each time the participant is asked to recall as many words as possible (immediate recall, maximal score = 40). After an interval of 15 min the participant is again asked to recall as many words as possible (delayed recall, maximal score = 8). For the last variable, the examiner reads aloud 16 words, which are the 8 words presented earlier and 8 new words. The participant is asked which words he/she recognizes from the list presented earlier (recognition, maximal score = 16).

Executive Function

This was assessed with 2 tests: the digit span test (both forward and backward) and the category fluency test.

(1) Digit span (forward and backward) [37]. In the digit span forward condition, the participant is asked to a repeat series of digits read out by the examiner. In the digit span backward condition, the participant is requested to repeat a series of digits in the reverse order. This subtest is known to load heavily on working memory. The outcome measure is the number of series correctly reproduced (maximal score = 12).

(2) Category fluency [38]. In this test the participant is asked to name as many animals and professions as he or she can within 1 min (for each). This test requires a strategic search mechanism to retrieve information from semantic memory. The outcome measure is the total number of animals and professions produced.

Statistical Analysis

Differences between groups at baseline were analyzed by independent-samples t tests, χ^2 tests or nonparametric Mann-Whitney U tests. Scores on neuropsychological tests were converted to z-scores and, according to a factor analysis, added up to form specific domains: a memory domain, an executive function domain and a total cognition domain. Neuropsychological tests were also analyzed separately. At baseline, the cognitive domains and all neuropsychological test variables were compared between groups by using independent-samples t tests. A linear mixed model was used to analyze differences between groups on the 3 domains and on the separate neuropsychological tests at the 3 assessments. This modeling technique accounts for the correlation between repeated measures and permits unequal numbers of assessments, resulting from loss to follow-up. The model was fitted for any clustering effects, since participants were clustered within nursing homes. Time was used as a within-subjects variable (T1–T2–T3) and group as the between-subjects variable (experimental-control). When significant time × group interactions were found, post-hoc interaction contrasts were determined, i.e. T1–T2, indicative for treatment effects, and T2–T3, indicative for long-term treatment effects [39]. To explain the interaction effects, paired-sample t tests were applied to evaluate differences within the experimental and control groups. In view of the exploratory nature of the study, separate paired-sample t tests were performed to investigate the effects on the test which was presumed to be most sensitive to improvement after this specific intervention, i.e. the face recognition test. When a lack of difference (in means and standard deviations) between 2 levels (baseline T1 and T3) could be demonstrated, means were pooled. The use of this procedure results in a considerable gain of discriminative power as compared to an overall F-statistic of an analysis of variance and has successfully been used previously [40]. Correcting for multiple analyses over the 8 cognitive variables, the Bonferroni correction was applied to the significance level of $p = 0.05$, which resulted in a critical value of $p = 0.006$. An alpha from 0.006 to 0.01 was considered a trend. All statistical analyses were performed using SPSS version 11.5 (SPSS, Inc., Chicago, Ill., USA).

Results

Participant Flow and Characteristics

From the 47 aged nursing home residents with dementia (45 women) who were enrolled in the study, 3 participants dropped out during the intervention (all experimental group) and denied further assessment. Three other participants did not want to finish the entire intervention but did undergo the assessment after the intervention (T2). Forty-four participants were included in the modified intention-to-treat analysis (experimental group n = 19, control group n = 25). Two participants withdrew consent during the last assessment (T3; 2 from the control group) and 1 from the experimental group became too ill to participate (fig. 1).

Table 1 compares baseline characteristics between groups. The mean age of all participants was 85.7 years and mean MMSE score was 17 (range 10–24). Groups did not differ significantly concerning age and mean MMSE score (table 1). There were no differences in gender and education between groups [$\chi^2(1) = 0.04$, $p = 0.84$, and $z = -0.21$, $p = 0.84$, respectively]. The types of diagnosis that were mentioned in the medical status were: AD (n = 7); vascular dementia (n = 6); combined AD and vascular dementia (n = 6), and dementia not further specified (n = 25). The distribution of subtypes of dementia did not differ between groups ($z = -0.96$, $p = 0.34$). Furthermore, groups did not differ in level of depression and anxiety (table 1). Specific conditions in the medical history of the participants included hypertension (n = 15), arthrosis (n = 10), diabetes mellitus (n = 9), cataract surgery (n = 8), peripheral vascular disease (n = 8), hernia (n = 7), atrial fibrillation (n = 6), decubitus ulcer (n = 5), hyper-/hypothyroidism (n = 5), myocardial infarction (n = 5) and tumors (n = 5). None of the main categories differed between groups (table 1), nor did total number of conditions ($z = -0.07$, $p = 0.94$). Cholinesterase inhibitors were not prescribed to any of the participants. There were no differences between groups in medication use (table 1). ApoE genotype could be assessed in 24 out of the 44 participants (54.5%): 7 participants (15.9%) were too ill or died before assessment, 4 of the participants' relevant relatives (9.1%) denied consent, and in 9 of the samples (20.4%) the amount

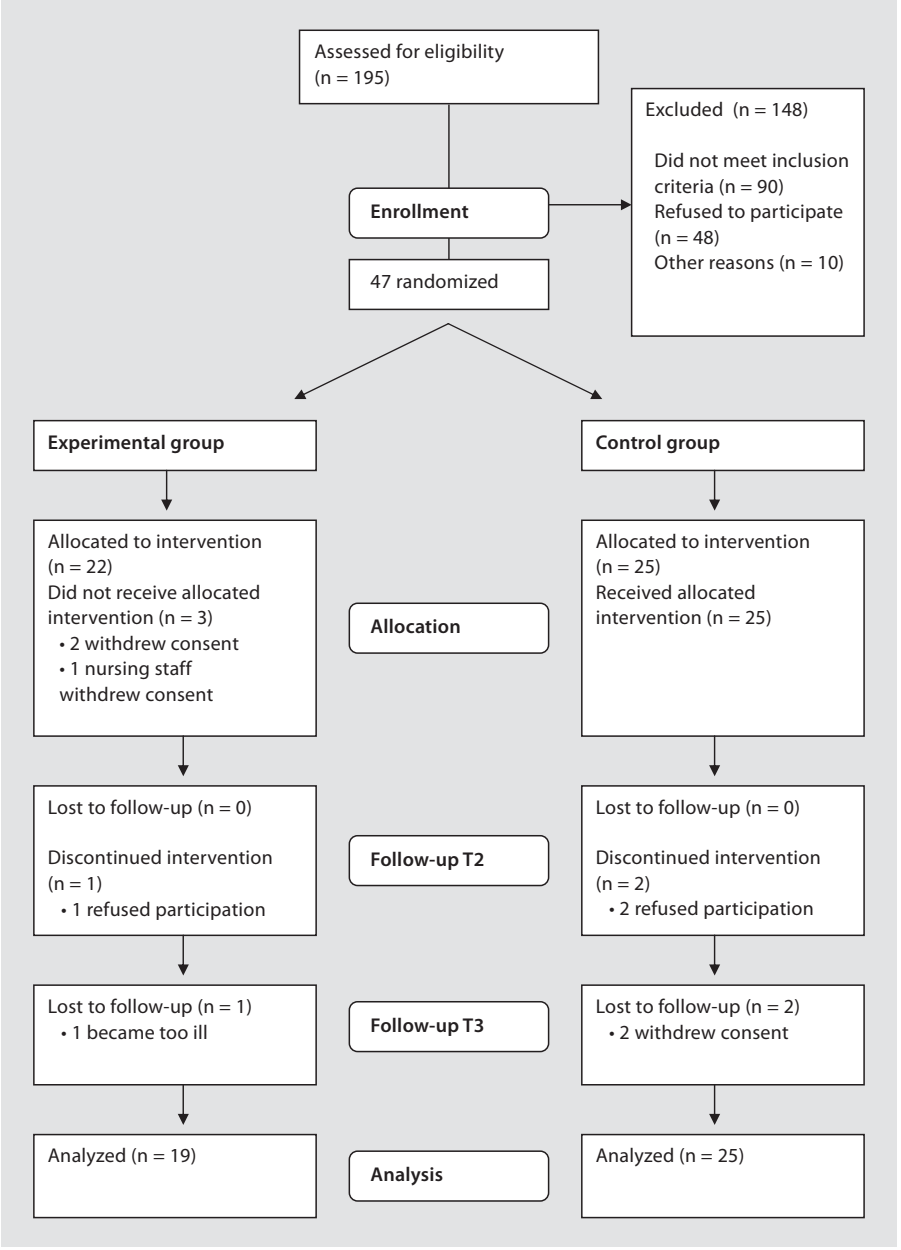

Fig. 1. Flowchart showing study design. T2 is the follow-up assessment at 6 weeks. T3 is the follow-up (delayed assessment) after 12 weeks.

of DNA isolated from the swab was too little to get a reliable result even after several attempts.

The level of amusement elicited by the tapes in the experimental group did not differ significantly from the tapes in the control condition ($z = -1.59$, $p = 0.11$).

Cognition

Means and standard deviations of the experimental and control group on the 3 different assessments are shown in table 2.

Memory Domain

A factor analysis revealed that the memory domain could best be formed by all subtests of the RBMT and the 8 words test, except for delayed recall variable on the 8 words test (Cronbach's alpha = 0.73). At baseline, there was no significant difference between groups [$t(42) = 1.55$, $p = 0.13$]. The mixed model analysis revealed no significant time × group interaction (table 3).

Table 2. Means and standard deviations of the independent variables

	Experimental group (n = 19)			Control group (n = 25)		
	T1	T2	T3	T1	T2	T3
Digit span forward	4.33 ± 1.37	5.22 ± 1.22	4.11 ± 1.71	4.87 ± 2.14	4.78 ± 1.61	4.83 ± 1.90
Digit span backward	4.22 ± 21.96	4.06 ± 1.55	3.50 ± 1.04	3.35 ± 1.61	3.22 ± 1.54	3.61 ± 1.73
Category fluency	14.29 ± 7.04	13.88 ± 7.04	14.71 ± 7.33	11.96 ± 6.11	11.13 ± 5.83	11.65 ± 6.22
RBMT faces	5.53 ± 2.60	6.94 ± 1.89	5.53 ± 2.50	4.35 ± 3.75	5.04 ± 3.66	5.48 ± 3.48
RBMT pictures	12.71 ± 5.79	12.12 ± 5.72	12.59 ± 4.52	10.61 ± 7.17	11.13 ± 7.36	11.22 ± 7.15
8WT immediate recall	18.00 ± 4.53	17.82 ± 4.56	19.06 ± 3.67	15.74 ± 4.39	16.09 ± 5.78	15.17 ± 7.25
8WT delayed recall	0.35 ± 0.70	0.41 ± 0.71	0.35 ± 0.79	0.35 ± 0.83	0.43 ± 1.20	0.39 ± 0.84
8WT recognition	11.06 ± 2.84	11.59 ± 2.21	11.30 ± 2.26	11.00 ± 2.43	10.86 ± 2.38	10.77 ± 2.25

8WT = Eight words test; RBMT = Rivermead Behavioral Memory Test; T = time (assessment).

Table 3. Mixed model F and p values for the 3 domains

	Time × group			Contrast[1] T1–T2					Contrast[1] T2–T3				
	F	d.f.	p	t	d.f.	p	Coef.	95% CI	t	d.f.	p	Coef.	95% CI
Memory domain	0.32	2, 39.48	0.73	0.49	44.00	0.63	0.09	–0.27, 0.44	0.31	34.58	0.76	0.04	–0.27, 0.44
EF domain	1.34	2, 42.89	0.27	–0.13	44.00	0.90	–0.02	–0.32, 0.28	1.58	40.06	0.12	0.28	–0.08, 0.63
Cognition domain	1.75	2, 43.11	0.19	–0.81	44.00	0.42	–0.08	–0.28, 0.12	1.87	42.54	0.07	0.20	–0.02, 0.42

Coef = Coefficient; EF = executive function; T = time (assessment).
[1] Interaction contrasts are defined as experimental vs. control group.

EF Domain

This was composed of the digit span backward and category fluency (Cronbach's alpha = 0.74). There was no significant difference between both groups at baseline [t(42) = 1.57, p = 0.13]. In the mixed model analysis no significant time × group interaction effect was found (table 3).

Total Cognition Domain

Scores on all the neuropsychological tests formed the total cognition domain (Cronbach's alpha = 0.74). At baseline, groups did not differ [t(42) = 1.37, p = 0.18]. Mixed model analysis did not show a significant time × group interaction effect (table 3).

Separate Neuropsychological Tests

None of the separate neuropsychological test variables differed significantly between groups at baseline ($0.10 < p < 0.83$). In the mixed model analysis, only the digit span forward variable showed a significant interaction effect [F(2,42.91) = 5.71, p = 0.006]. The contrast that was indicative for treatment effects (T1–T2) did not turn out to be significant, but showed a trend [t(44) = –2.73, p = 0.009]. The experimental group showed improved performance after the intervention period [t(18) = –3.62, p = 0.002], whereas the control group did not [t(24) = 0.46, p = 0.65]. With respect to the face recognition test, linear mixed model analysis did not show a significant interaction effect [F(2,42.45) = 1.62, p = 0.21]. However, a paired-sample t test, using T1–T3 pooled means, revealed a significant improvement in the experimental group [t(16) = 3.17, p = 0.006]. Results could not be pooled for the control group since T1 and T3 assessments were not similar. Paired-sample t test comparing T1 and T2 of the control group did not turn out to be significant [t(24) = –1.00, p = 0.33].

Discussion

Although in the present pilot study we did not observe an overall positive effect of the observation of hand motor activity on the different cognitive domains in nursing home residents with dementia, specific cognitive functions seem to be more sensitive to the intervention than others. One significant interaction effect was found on the digit span forward subtest, which is a measure of general attention [37]. The experimental group showed an improved performance on this test. Additionally, comparison of the pooled means of the T1 and T3 assessment compared to T2 assessment on the face recognition test showed an interesting result. Performance in the experimental group improved, whereas the performance in the control group did not. A possible explanation for this finding may be that, as stated earlier, the area surrounding the superior temporal sulcus, involved in the recognition of faces, and known to include mirror neurons, is activated by observing hand movements [20]. One might speculate that activation of this area in the experimental condition has stimulated the superior longitudinal fasciculus, involving connections between the superior temporal regions, the parietal cortex and the frontal cortex [14, 15, 41]. It is noteworthy that the superior temporal/parietal regions, in turn, play an important role in attention [42], which may provide a possible explanation for the improved digit span forward score.

In future research one may try to extend the video intervention to optimize its possible beneficial effect on cognition. One may consider including imitation of the observed hand movements, since this activity activates mirror neurons to a larger degree [43]. Also, activation of mirror neurons is stronger during the observation of 'live' hand movements compared to observing those on video [28]. Be that as it may, observation of hand movements on video activates mirror neurons in several studies [12, 13]. Besides, merely observing a video may enhance the suitability of the intervention for the current population. More specifically, older persons in a nursing home setting may be limited in their ability to perform hand motor activities [6]. An intervention is also more applicable when movements are observed on video rather than in real life. Watching videos, both alone and in a group, proved to be an appropriate activity for older persons with dementia [44]. A possibility to increase the effect on cognition could be applying videotapes involving additional movements, e.g. bending of the torso, movements of the head and arms, and particularly movements of the mouth [12, 45]. In addition, videotapes may be adapted to the specific interests of the target group, for instance by including elements of former jobs or hobbies. To investigate to what degree these proposed interventions would activate mirror neurons in older persons with dementia, neuro-imaging studies are a prerequisite.

The choice of the control videos warrants attention. We selected control videos that showed a documentary of the Dutch provinces and included short interviews, to attempt to control for the verbal conversation element in the hand movement videos. This element, however, may have stimulated the area around the superior temporal sulcus as well, since this area is also sensitive to moving bodies and expressive gestures [46], elements that were present in the control videotapes. Therefore, the control videotapes in the current study may not have been ideal. Instead, a documentary on scenery and landscapes without the presence of humans/animals may be a better choice. Additionally, although there was no significant difference in the level of interest for the videotapes of both conditions, the small questionnaire used in the present study was not validated for the population. Since impairments in verbal comprehension are common in dementia [47], it is recommended that in future studies, verbal comprehension should be assessed to make sure such a questionnaire is correctly understood.

One limitation of the present study is the lack of knowledge to what degree the participants paid attention to the videotapes. It is well-known that older persons with dementia have a limited attention span [48]. For this reason, the students that attended the intervention were carefully instructed to try to keep the participants focused on the screen as much as possible. When the participants' gaze was directed to the screen however, it remains unknown whether focus was actually directed at the hand movements. Future studies may consider use of portable eye-trackers to determine exact direction of the gaze [49].

A second limitation of the present pilot study is the lack of determination of the ApoE genotype in all participants. The presence of an ApoE4 allele is a risk factor for AD [50] and may modify the effects of motor activity on cognition. Support for this notion comes from studies investigating the effects of pharmacological interventions, i.e. cholinesterase-inhibitors. The specific role of the ApoE4 allele is, however, controversial since results have been inconsistent [51, 52]. In addition, epidemiological studies have shown that the relationship between physical activity and cognition in older adults was either especially apparent in ApoE4 carriers [53], or in ApoE4

noncarriers [54]. Notably, the presence of an ApoE4 allele may be accompanied by a diminished metabolic activity in the cholinergic nucleus basalis of Meynert, not only in persons with AD [55, 56] but also in controls [55, 57]. Activity differences in this system may interfere with many cortical processes [55]. All in all, although the precise role of the ApoE genotype is unclear, presence of the ApoE4 allele may have influenced study outcome. Exploration of the precise role of the ApoE genotype in response to non-pharmacological intervention studies should be the focus of future research efforts.

In sum, although this pilot study does not show an overall positive effect of movement observation on cognition in nursing home residents with dementia, the results do suggest that hand movement observation might exert a beneficial effect on face recognition. Use of videotapes may offer an easily applicable type of intervention in the nursing home setting. Additionally, optimizing the level of activation of brain areas that are part of the mirror neuron system could be of clinical importance and should therefore be the focus of future studies. These studies, using larger sample sizes, could present firm conclusions about the effectiveness of hand movement observation on cognition in older persons with dementia.

Acknowledgments

Thanks to Nienke Postma, Maria Koster and Jacqueline Sluijs for help with the ApoE genotyping. We are grateful to Fontis Amsterdam and Alzheimer Nederland for financially supporting this project.

References

1 Kramer AF, Hahn S, Cohen NJ, Banich MT, McAuley E, Harrison CR, Chason J, Vakil E, Bardell L, Boileau RA, Colcombe A: Ageing, fitness and neurocognitive function. Nature 1999;400:418–419.

2 Eggermont L, Swaab D, Luiten P, Scherder E: Exercise, cognition and Alzheimer's disease: more is not necessarily better. Neurosci Biobehav Rev 2006;30:562–575.

3 Ang YH, Au SY, Yap LK, Ee CH: Functional decline of the elderly in a nursing home. Singapore Med J 2006;47:219–224.

4 Scherder EJ, Van Paasschen J, Deijen JB, Van Der Knokke S, Orlebeke JF, Burgers I, Devriese PP, Swaab DF, Sergeant JA: Physical activity and executive functions in the elderly with mild cognitive impairment. Aging Ment Health 2005;9:272–280.

5 Davis KD, Taylor SJ, Crawley AP, Wood ML, Mikulis DJ: Functional MRI of pain- and attention-related activations in the human cingulate cortex. J Neurophysiol 1997;77:3370–3380.

6 Carmeli E, Patish H, Coleman R: The aging hand. J Gerontol A Biol Sci Med Sci 2003;58:146–152.

7 Kluger A, Gianutsos JG, Golomb J, Ferris SH, George AE, Franssen E, Reisberg B: Patterns of motor impairement in normal aging, mild cognitive decline, and early Alzheimer's disease. J Gerontol B Psychol Sci Soc Sci 1997;52:P28–P39.

8 Rizzolatti G, Fadiga L, Gallese V, Fogassi L: Premotor cortex and the recognition of motor actions. Brain Res Cogn Brain Res 1996;3:131–141.

9 Fecteau S, Pascual-Leone A, Théoret H: Psychopathy and the mirror neuron system: preliminary findings from a non-psychiatric sample. Psychiatry Res 2008;160:137–144.

10 Collins JW: The neuroscience of learning. J Neurosci Nurs 2007;39:305–310.

11 Buccino G, Solodkin A, Small SL: Functions of the mirror neuron system: implications for neurorehabilitation. Cogn Behav Neurol 2006;19:55–63.

12 Buccino G, Binkofski F, Fink GR, Fadiga L, Fogassi L, Gallese V, Seitz RJ, Zilles K, Rizzolatti G, Freund HJ: Action observation activates premotor and parietal areas in a somatotopic manner: an fMRI study. Eur J Neurosci 2001;13:400–404.

13 Buccino G, Vogt S, Ritzl A, Fink GR, Zilles K, Freund HJ, Rizzolatti G: Neural circuits underlying imitation learning of hand actions: an event-related fMRI study. Neuron 2004;42:323–334.

14 Bürgel U, Amunts K, Hoemke L, Mohlberg H, Gilsbach JM, Zilles K: White matter fiber tracts of the human brain: three-dimensional mapping at microscopic resolution, topography and intersubject variability. Neuroimage 2006;29:1092–1105.

15 Schmahmann JD, Pandya DN, Wang R, Dai G, D'Arceuil HE, de Crespigny AJ, Wedeen VJ: Association fibre pathways of the brain: parallel observations from diffusion spectrum imaging and autoradiography. Brain 2007;130:630–653.

16 Iacoboni M: Neural mechanisms of imitation. Curr Opin Neurobiol 2005;15:632–637.

17 Wang K, Liang M, Wang L, Tian L, Zhang X, Li K, Jiang T: Altered functional connectivity in early Alzheimer's disease: a resting-state fMRI study. Hum Brain Mapp 2007;28:967–978.

18 Stam CJ, Jones BF, Manshanden I, van Cappellen van Walsum AM, Montez T, Verbunt JP, de Munck JC, van Dijk BW, Berendse HW, Scheltens P: Magnetoencephalographic evaluation of resting-state functional connectivity in Alzheimer's disease. Neuroimage 2006;32:1335–1344.

19 Goethals I, Audenaert K, Van de Wiele C, Dierckx R: The prefrontal cortex: insights from functional neuroimaging using cognitive activation tasks. J Neuropathol Exp Neurol 2004;31:408–416.

20 Haxby JV, Hoffman EA, Gobbini MI: The distributed human neural system for face perception. Trends Cogn Sci 2000;4:223–233.

21 Kohler CG, Anselmo-Gallagher G, Bilker W, Karlawish J, Gur RE, Clark CM: Emotion-discrimination deficits in mild Alzheimer disease. Am J Geriatr Psychiatry 2005;13:926–933.

22 Bokde AL, Lopez-Bayo P, Meindl T, Pechler S, Born C, Faltraco F, Teipel SJ, Möller HJ, Hampel H: Functional connectivity of the fusiform gyrus during a face-matching task in subjects with mild cognitive impairment. Brain 2006;129:1113–1124.

23 Fratiglioni L, Paillard-Borg S, Winblad B: An active and socially integrated lifestyle in late life might protect against dementia. Lancet Neurol 2004;3:343–353.

24 Verghese J, Lipton RB, Katz MJ, Hall CB, Derby CA, Kuslansky G, Ambrose AF, Sliwinski M, Buschke H: Leisure activities and the risk of dementia in the elderly. N Engl J Med 2003;348:2508–2516.

25 Avila R, Carvalho IA, Bottino CM, Miotto EC: Neuropsychological rehabilitation in mild and moderate Alzheimer's disease patients. Behav Neurol 2007;18:225–233.

26 Davis RN, Massman PJ, Doody RS: Cognitive intervention in Alzheimer disease: a randomized placebo-controlled study. Alzheimer Dis Assoc Disord 2001;15:1–9.

27 Mate-kole CC, Fellows RP, Said PC, McDougal J, Catayong K, Dang V, Gianesini J: Use of computer assisted and interactive cognitive training programmes with moderate to severely demented individuals: a preliminary study. Aging Ment Health 2007;11:485–495.

28 Järveläinen J, Schurmann M, Avikainen S, Hari R: Stronger reactivity of the human primary motor cortex during observation of live rather than video motor acts. Neuroreport 2001;12:3493–3495.

29 Folstein MF, Folstein SE, McHugh PR: Mini-Mental State: practical method for grading cognitive state of patients for clinician. J Psychiatr Res 1975;12:189–198.

30 Kok RM, Heeren ThJ, van Hemert AM: De Geriatric Depression Scale (in Dutch). Tijdschrift voor Psychiatrie 1993;35:416–421.

31 Arrindell, WA, Ettema JH: SCL-90. Handleiding bij een multidimensionele psychopathologie-indicator. Lisse, Swets & Zeitlinger, 1986.

32 Ilveskoski E, Lehtimaki T, Erkinjuntti T, Koivula T, Karhunen PJ: Rapid apolipoprotein E genotyping from mailed buccal swabs. J Neurosci Methods 1998;79:5–8.

33 Gioia L, Vogt LJ, Freeman WM, Flood A, Vogt BA, Vrana KE: PCR-based apolipoprotein E genotype analysis from archival fixed brain. J Neurosci Methods 1998;80:209–214.

34 Ten Brinke W, De Jong C, Loeven B, Beulink C, Krauwer M: De 12 provincies. Utrecht, Teleac, 1989.

35 Wilson B, Cockburn J, Baddeley A: The Rivermead Behavioural Memory Test. Titchfield, Thames Valley Test Company, 1987.

36 Lindeboom J, Jonker C: Amsterdamse Dementie-screeningtest, handleiding. Lisse, Swets & Zeitlinger, 1989.

37 Wechsler, D: Wechsler Memory Scale – Revised. New York, The Psychological Corporation, 1987.

38 Snijders JT, Verhage F: Groninger Intelligentie Test. Lisse, Swets & Zeitlinger, 1983.

39 Fitzmaurice GM, Laird NM, Ware JH: Applied Longitudinal Analysis. Hoboken, Wiley-Interscience, 2004.

40 Van Someren EJ, Scherder EJ, Swaab DF: Transcutaneous electrical nerve stimulation (TENS) improves circadian rhythm disturbances in Alzheimer disease. Alzheimer Dis Assoc Disord 1998;12:114–118.

41 Rizzolatti G: The mirror neuron system and imitation; in Hurley S, Chater N (eds): Perspectives on Imitation: From Neuroscience to Social Science. London, MIT Press, 2005, pp 55–76.

42 Weissman DH, Woldorff MG: Hemispheric asymmetries for different components of global/local attention occur in distinct temporo-parietal loci. Cereb Cortex 2005;15:870–876.

43 Iacoboni M, Woods RP, Brass M, Bekkering H, Mazziotta JC, Rizzolatti G: Cortical mechanisms of human imitation. Science 1999;286:2526–2528.

44 Lund DA, Hill RD, Caserta MS, Wright SD: Video respite: an innovative resource for family, professional caregivers, and persons with dementia. Gerontologist 1995;35:683–687.

45 Nishitani N, Hari R: Viewing lip forms: cortical dynamics. Neuron 2002;36:1211–1220.

46 Barraclough NE, Xiao D, Oram MW, Perrett DI: The sensitivity of primate STS neurons to walking sequences and to the degree of articulation in static images. Prog Brain Res 2006;154:135–148.

47 Rogers TT, Ivanoiu A, Patterson K, Hodges JR: Semantic memory in Alzheimer's disease and the frontotemporal dementias: a longitudinal study of 236 patients. Neuropsychology 2006;20:319–335.

48 Perry RJ, Watson P, Hodges JR: The nature and staging of attention dysfunction in early (minimal and mild) Alzheimer's disease: relationship to episodic and semantic memory impairment. Neuropsychologia 2000;38:252–271.

49 Geruschat DR, Hassan SE, Turano KA: Gaze behavior while crossing complex intersections. Optom Vis Sci 2003;80:515–528.

50 Corder EH, Saunders AM, Strittmatter WJ, Schmechel DE, Gaskell PC, Small GW, Roses AD, Haines JL, Pericak-Vance MA: Gene dose of apolipoprotein E type-4 allele and the risk of Alzheimer's disease in late-onset families. Science 1993;261:921–923.

51 Bizzarro A, Marra C, Acciarri A, Valenza A, Tiziano FD, Brahe C, Masullo C: Apolipoprotein E epsilon4 allele differentiates the clinical response to donepezil in Alzheimer's disease. Dement Geriatr Cogn Disord 2005;20:254–261.

52 Visser PJ, Scheltens P, Pelgrim E, Verhey FR; Dutch ENA-NL-01 Study Group: Medial temporal lobe atrophy and APOE genotype do not predict cognitive improvement upon treatment with rivastigmine in Alzheimer's disease patients. Dement Geriatr Cogn Disord 2005;19:126–133.

53 Rovio S, Kareholt I, Helkala EL, Viitanen M, Winblad B, Tuomilehto J, Soininen H, Nissinen A, Kivipelto M: Leisure-time physical activity at midlife and the risk of dementia and Alzheimer's disease. Lancet Neurol 2005;4:705–711.

54 Podewils LJ, Guallar E, Kuller LH, Fried LP, Lopez OL, Carlson M, Lyketsos CG: Physical activity, APOE genotype, and dementia risk: findings from the Cardiovascular Health Cognition Study. Am J Epidemiol 2005;161:639–651.

55 Salehi A, Dubelaar EJ, Mulder M, Swaab DF: Decreased activity of nucleus basalis neurons in Alzheimer's disease is ApoE type dependent. Proc Natl Acad Sci USA 1998;95:11445–11449.

56 Dubelaar EJ, Verwer RW, Hofman MA, Van Heerikhuize JJ, Ravid R, Swaab DF: ApoE epsilon4 genotype is accompanied by lower metabolic activity in nucleus basalis of Meynert neurons in Alzheimer patients and controls as indicated by the size of the Golgi apparatus. J Neuropathol Exp Neurol 2004;63:159–169.

57 Reiman EM, Chen K, Alexander GE, Caselli RJ, Bandy D, Osborne D, Saunders AM, Hardy J: Functional brain abnormalities in young adults at genetic risk for late-onset Alzheimer's dementia. Proc Natl Acad Sci USA 2004;101:284–289.